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# LETTERS TO THE EDITOR

## Antimicrobial therapy in pneumococcal meningitis: an epidemiological assessment from Turkey

*Streptococcus pneumoniae* is the single most important cause of acute purulent meningitis, occurring in 47% of cases of acute bacterial meningitis.[1] To the authors' knowledge, there are no published data on the treatment of pneumococcal meningitis based on local epidemiological studies in Turkey. In this letter we refer to recent and current pneumococcal studies carried out in accordance with the National Committee for Clinical Laboratory Standards. Only the susceptibility test results of pathogenic pneumococci are taken into account; resistance patterns of those obtained from carriers are excluded. The epidemiological data from which the therapeutic options for pneumococcal meningitis are derived are presented in Table 1.

Approximately 40% of pneumococci are now penicillin resistant and in Turkey 20% of resistant isolates are high-level penicillin resistant.[2] For this reason penicillin is no longer the best choice for the treatment of pneumococcal meningitis.

Third generation cephalosporins (e.g. ceftriaxone or cefotaxime) are another possible therapeutic option when pneumococcus is the probable cause of infection. Ten studies on the susceptibility patterns of pathogenic pneumococci for third generation cephalosporins have been carried out in Turkey.[3—6] Six of them, completed since 2000, reported ceftriaxone and cefotaxime resistances not exceeding 2.3%.[5,6] Moreover, in one study over the period 1998—2000, all of the isolates were susceptible to cefepime. Seventy-six penicillin-resistant pneumococci isolated between 1997 and 2001 were evaluated in a reference laboratory in Ankara.[7] Only four of these isolates (5.3%) were found to be cefotaxime-resistant. Consequently, third generation cephalosporins, ceftriaxone and cefotaxime in particular, are the antibacterial agents of choice in the treatment of pneumococcal meningitis in Turkey.

Vancomycin resistance in pneumococci has not been reported in Turkish studies.[2] If a community is known to have significant cephalosporin resistance (minimum inhibitory concentration $>0.5\ \mu g/mL$) in more than 3% of invasive pneumococci, vancomycin should be added to the third-generation cephalosporin.[8,9] No recent Turkish studies show resistance rates which exceed the probable threshold of 3% for additional vancomycin use. In our opinion, updating of current data is required; empirical vancomycin administration in probable pneumococcal meningitis is unnecessary, but its use in Turkey is not far off.

Two carbapenems, imipenem and meropenem, have been extensively studied in patients with bacterial meningitis. Unfortunately, carbapenem activity against pneumococci has been little investigated in Turkey. A study published in 1996 mentions 2.2% resistance to imipenem and another completed in 2000 shows no imipenem resistance.

The fluoroquinolones have undergone extensive study in experimental animal models of penicillin-resistant pneumococcal meningitis. Currently, the recommended quinolones in the treatment of acute bacterial meningitis are gatifloxacin and moxifloxacin. Data derived from recent local Turkish studies show no resistance to levofloxacin, grepafloxacin, gemifloxacin and moxifloxacin.[5,6,10] The $MIC_{90}$ of gemifloxacin was found to be 2-fold lower than that of moxifloxacin and 32-fold lower than those of ciprofloxacin and levofloxacin.[5] According to these results, newer fluoroquinolones would also appear to be acceptable alternatives in the treatment of pneumococcal meningitis. Moreover, newer fluoroquinolones act synergistically with vancomycin and beta-lactam antibiotics against penicillin-resistant pneumococcal meningitis in experimental rabbit meningitis, potentially providing a new therapeutic strategy. In one report the combination of ceftriaxone with levofloxacin and in another cefotaxime with levofloxacin, acted synergistically in experimental pneumococcal meningitis and overcame the risks of quinolone-induced resistance.[11,12] Similarly, meropenem combined with levofloxacin provided synergism and sterilized the CSF in a rabbit model of pneumococcal meningitis.[13] Epidemiological data in Turkey would suggest that these approaches must perhaps be spared for the future, when extended spectrum cephalosporin resistance rates are more elevated.

Chloramphenicol, which has been in use for a long time, has been recommended for the treatment of acute bacterial meningitis due to its relatively low cost, which makes it more accessible to communities with limited resources. In recent local Turkish studies, chloramphenicol resistance patterns were found to be less than 10% and this drug, alone or in combination, may be regarded as an alternative option. Trimethoprim—sulfamethoxazole is one of the most evaluated antibiotics in Turkey. Local research undertaken from 2000 on, shows trimethoprim—sulfamethoxazole resistance

**Table 1** Studies on antibiotic resistance in pneumococci

| Period [a] | Isolates (*N*) | CTXM | CFXN | RIF | IMP | LEVO | GRP | GEMI | MOXI | CLA | SXT |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1993–96 [3] | 143 | 2% | | | | | | | | 4% | |
| 1996 | 312 | | | | 2.2% | | | | | | |
| 1996 | 84 | | 0% | | | | | | | 0% | |
| 1997 | 68 | 0% | 0% | | | | | | | 9% | 28% |
| 1996–98 [4] | 80 | | 6.25% | | | | | | | | |
| 1997–2000 | 101 | 0% | 0% | | | | | | | | |
| 1997–2000 | 42 | | | | 0% | 0% | 0% | | | | |
| 1997–2000 | 21 | 0% | 0% | | | | | | | | 81% |
| 1999–2001 [5] | 83 | | 0% | | | 0% | 0% | 0% | | | |
| 1999–2000 [6] | 142 | | 2.3% | | | 0% | | | | | 90% |
| 1999–2001 | 51 | | 1.96% | | | | | | | | 37.2% |
| 1999–2001 | 212 | | 2.3% | 2.1% | | | | | | 2.3% | |
| 2000–2001 [10] | 85 | | | | | 0% | | | | | 46% |
| 2001 | 40 | | | 0% | | 0% | | | | | 40% |
| 2002 | 43 | | | | | | | | | 3.6% | 44% |

CTXM: cefotaxime; CFXN: ceftriaxone; RIF: rifampin; IMP: imipenem; LEVO: levofloxacin; GRP: grepafloxacin; GEMI: gemifloxacin; MOXI: moxifloxacin; CLA: chloramphenicol; SXT: trimethoprim–sulfamethoxazole.

[a] References not cited here can be found online – see Appendix A.

rates up to 50%,[6,10] i.e., it should not be used as an empirical option in probable pneumococcal meningitis.

Continued surveillance of antibiotic resistance patterns in general and particularly in third generation cephalosporins are key strategies in Turkey for the treatment of pneumococcal meningitis.

*Conflict of interest*: No competing interest declared.

## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2005.03.009.

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